

**2014 Annual Report
on Inspections of
Establishments**

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Introduction

On July 9, 2012, the Food and Drug Administration Safety and Innovation Act (FDASIA) (Public Law 112-144) was signed into law. FDASIA section 705 amends section 510(h) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 USC 360(h)) to require, among other things, that FDA make reports on inspections of registered establishments available on an annual basis through the Agency's website. Section 510(h)(6) of the FD&C Act states:

ANNUAL REPORT ON INSPECTIONS OF ESTABLISHMENTS.

Beginning in 2014, not later than February 1 of each year; the Secretary shall make available on the Internet Web site of the Food and Drug Administration a report regarding--

(A)(i) the number of domestic and foreign establishments registered pursuant to this section in the previous fiscal year; and

(ii) the number of such domestic establishments and the number of such foreign establishments that the Secretary inspected in the previous fiscal year;

(B) with respect to establishments that manufacture, prepare, propagate, compound, or process an active ingredient of a drug, a finished drug product, or an excipient of a drug, the number of each such type of establishment; and

(C) the percentage of the budget of the Food and Drug Administration used to fund the inspections described under subparagraph (A).

This report satisfies the Annual Report requirement for Fiscal Year (FY) 2013.

Data Collection and Definitions

The FDA product Centers included in this Annual Report are the Center for Biologics Evaluation and Research (CBER), the Center for Drug Evaluation and Research (CDER), the Center for Veterinary Medicine (CVM), and the Center for Devices and Radiological Health (CDRH).¹

Data for the registration information contained in this report were generated by FDA's registration databases for FY 2013. Data for the inspection information contained in this report were generated from the Office of Regulatory Affairs' (ORA) Field Accomplishments and Compliance Tracking System (FACTS). The data consist of the numbers of inspections conducted at drug and device establishments to evaluate compliance with Good Manufacturing Practice (GMP), including both Current Good Manufacturing Practice (CGMP) for drugs and Quality Systems (QS) regulations for devices, as applicable (hereafter referred to as "GMP inspection(s)"). The hours of work spent preparing for, conducting, and documenting GMP inspections, as reported into FACTS by FDA staff, were used to calculate the percentage of ORA's field medical product budget authority that supported those inspections.

Tables 1, 2, and 4 show data about both drug and device establishments; Table 3 shows data about drug establishments only. As noted above, the numbers reported in Table 2 are for GMP inspections only. However, registered drug and device establishments are subject to other types of inspections, such as product-specific only, pre-approval inspections for drugs. Therefore, while Table 1 shows registered drug and device establishments, Table 2 shows a subset of the types of inspections FDA may conduct at those establishments, i.e., GMP inspections. Table 4 shows the percentage of the ORA field medical product budget authority involved in conducting domestic and foreign drug and device establishment GMP inspections.

¹ For more information on the FDA product Centers and Office of Regulatory Affairs, see <http://www.fda.gov/aboutFDA/Centersoffices/default.htm>.

Section 510(h)(6)(A)(i)–Number of Domestic and Foreign Establishments Registered Pursuant to Section 510 in FY 2013²

As of September 30, 2013, 9,120 domestic drug³ establishments and 12,468 domestic device⁴ establishments were registered pursuant to section 510 of the FD&C Act, for a total of 21,588 registered domestic establishments. As of September 30, 2013, 3,493 foreign drug establishments and 9,385 foreign device establishments were registered pursuant to section 510, for a total of 12,878 registered foreign establishments. In all, there are 12,613 registered drug establishments (domestic and foreign), and 21,853 registered device establishments (domestic and foreign), totaling 34,466 registered establishments around the world.

TABLE 1			
Number of Registered Drug and Device Establishments			
	Domestic	Foreign	Total
Drug Establishments Registered	9,120	3,493	12,613
Device Establishments Registered	12,468	9,385	21,853
Total Drug and Device Establishments Registered	21,588	12,878	34,466

Section 510(h)(6)(A)(ii)–Number of Domestic and Foreign Establishments Inspected in FY 2013

² Section 510 of the FD&C Act requires manufacturers, repackers, and relabelers that engage in the manufacture, preparation, propagation, compounding, or processing of human or veterinary drugs, including human biological products, and devices to register their establishment(s) and submit a listing of every product in commercial distribution with the FDA. This information helps FDA maintain a catalog of all human and veterinary drugs, including biologics, and devices in commercial distribution in the United States. Many drug and device establishments that register with FDA do so voluntarily and are not obligated to be inspected by FDA. FDA uses the Official Establishment Inventory, a database maintained by ORA, as well as other databases to identify the subset of registered establishments that are subject to inspection.

³ "Drug" means (A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any articles specified in clause (A), (B), or (C). Section 201(g) of the FD&C Act (21 USC 321(g)).

⁴ "Device" means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is (1) recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them, (2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or (3) intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. Section 201(h) of the FD&C Act (21 USC 321(h)).

As of November 20, 2013, there have been 4,858 domestic GMP inspections of registered drug and device establishments and 1,138 foreign GMP inspections of registered drug and device establishments in FY 2013, for a total of 5,996 GMP inspections conducted in FY 2013.⁵ These inspection numbers include CGMP inspections for drugs⁶ and QS inspections for Class II and Class III devices.⁷

TABLE 2		
GMP Inspections of Registered Domestic and Foreign Drug and Device Establishments in FY 2013		
Domestic	Foreign	Total
4,858	1,138	5,996

⁵ The number of GMP inspections does not include other types of inspections that FDA conducts, such as product-specific only, pre-approval inspections of drug establishments and inspections of Class I device establishments.

⁶ The number of inspections of animal drug establishments includes GMP inspections of some non-registered facilities and inspections that are conducted by states under a contract with FDA.

⁷ Domestic device establishments engaged in the manufacture, propagation, compounding, or processing of a class II or class III medical device are subject to biennial inspection under 510(h)(2) of the FD&C Act.

Section 510(h)(6)(B)–Number of Registered Drug Establishments by Type⁸

As of September 30, 2013, 4,360 establishments were registered as finished drug product (FDP) establishments⁹ and 1,248 establishments were registered as active pharmaceutical ingredient (API) establishments¹⁰ pursuant to section 510 of the FD&C Act.¹¹

TABLE 3			
Type of Registered Drug Establishments			
FDP	API	Other ¹²	Total
4,360	1,248	7,005	12,613

⁸ Currently, FDA’s registration databases do not collect information regarding establishments that manufacture, prepare, propagate, compound or process only excipients; therefore those establishments are not captured in this category.

⁹ For the purposes of this report, we are considering the term “finished drug product” as it appears in Section 510(h)(6)(B) to mean “drug product” as defined in 21 CFR 210.3(b)(4): “a finished dosage form, for example, tablet, capsule, or solution, that contains a drug substance, generally, but not necessarily, in association with one or more ingredients.”

¹⁰ For the purposes of this report, we are considering the term "active ingredient" as it appears in Section 510(h)(6)(B) to mean "active pharmaceutical ingredient" as defined in Guidance for Industry: Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients: “Any substance or mixture of substances intended to be used in the manufacture of a drug product and that, when used in the production of a drug, becomes an active ingredient of the drug product. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and function of the body.”

¹¹ If an establishment manufactures, prepares, propagates, compounds, or processes both FDP and API, it is counted as a FDP establishment. API establishments are involved solely in the production of an API. The data sources for the FDP and API establishments reported in Table 3 are the registration databases maintained by CDER and CVM, currently the only drug registration data sources that include such information. Establishments that produce certain types of biological products register through the registration system maintained by CDER.

¹² This category includes, but is not limited to, establishments that manufacture, prepare, propagate, compound or process medical gases and medicated feed; and establishments that register through the registration system maintained by CBER.

Section 510(h)(6)(C)–Percentage of FDA Budget Used to Fund Establishment Inspections

FDA is able to provide the percentage of ORA’s field medical product program resources involved in conducting domestic and foreign drug and device establishment GMP inspections.¹³ The ORA total budget authority for FY 2013 is \$874,453,000.

Approximately \$250,192,000 of the ORA total budget authority is devoted to field medical product programs (hereafter “field medical product budget authority”), while the remaining \$624,261,000 is devoted to other product field programs (e.g., foods).¹⁴ The field medical product budget authority includes all field activities that support FDA’s biologics, human drugs, animal drugs, and medical device programs by assessing compliance with applicable laws and regulations. These activities include inspecting establishments, conducting sample analyses, examining products offered for entry into the United States, and certain emergency preparedness and response activities for FDA regulated medical products. Of the \$250,192,000, \$117,000,000 was used for domestic drug and device establishment GMP inspections, and \$46,000,000 was used for foreign drug and device establishment GMP inspections. These numbers are derived from the total FDA investigator and laboratory analyst hours reported into FACTS for those inspections. The estimated cost of these hours was then used to calculate the percentage of the field medical product budget authority used for both domestic and foreign drug and device establishment GMP inspections.¹⁵ As of November 20, 2013, for FY 2013 the percentage of the field medical product budget authority used to fund domestic drug and device establishment GMP inspections is approximately 46.76 percent.¹⁶ The percentage of the field medical product budget authority used to fund foreign drug and device establishment GMP inspections is approximately 18.39 percent.

TABLE 4		
Percentage of Field Medical Product Budget Authority Used for GMP Inspections		
Domestic	Foreign	Total
46.76%	18.39%	65.15%

¹³ In addition to GMP inspections, ORA conducts many other types of inspections such as product-specific only pre-approval inspections, Good Laboratory Practice inspections, bioequivalence inspections and inspections of clinical investigators, institutional review boards, and application sponsors.

¹⁴ The total field medical product budget authority is calculated by adding the budget authority for human drugs; biologics; animal drugs; and devices and radiological health field programs. This calculation assumes that field animal drug programs comprise 15 percent of the total field animal drugs and feed budget authority.

¹⁵ These percentages are based solely on the estimated cost for FY 2013 of field program resources of ORA. Field program resources include operational costs, such as onsite inspections of establishments and support personnel. These percentages do not include other resources related to the reported inspections, such as resources utilized in resulting compliance or enforcement activities involving inspected establishments.

¹⁶ This percentage does not include inspections of animal drug establishments conducted by the states under a contract with FDA.